DESCRIPTION OF REQUIREMENT

a. Objectives and Desired Results

The overall objective of the LTRC is to enable better management of lung diseases by increasing understanding of the pathogenetic mechanisms of these diseases through molecular histopathological studies of human lung tissues with and without disease. Primary emphases will be on chronic obstructive pulmonary disease (COPD) and idiopathic pulmonary fibrosis; secondary objectives may address other pulmonary diseases. The LTRC will collect lung tissue specimens, with corresponding clinical data from donor subjects, and make available these collections to lung disease researchers. Priority will be given to the collection of specimens that can be divided or replicated for distribution to many investigators. Clinical Centers of the LTRC will be eligible to obtain additional funding to carry out related research that utilizes LTRC specimens.

Specimens and clinical data appropriate to specific diseases will be collected from approximately 810-1620 donor subjects. It is anticipated that donor subjects will be enrolled at a rate of 3-6 per month at each of the Clinical Centers over a 54 month period.

b. Background Information

Chronic diseases of the lung are a major cause of death and disability among Americans. Some of these diseases are highly prevalent. For example, chronic obstructive pulmonary disease (COPD) affects over 15 million people in this country and is now the fourth leading cause of death. Other lung diseases are less common but are very severe. For example, idiopathic pulmonary fibrosis has a prevalence of approximately 28 cases per 100,000 and is associated with 50-70% mortality at 5 years after diagnosis. Chronic pulmonary diseases tend to be: 1) associated with an inflammatory process in the lungs; 2) progressive; 3) inadequately controlled by current therapies, and 4) poorly understood in terms of pathogenetic mechanisms. Research is needed that will foster the development of novel therapeutic approaches for these conditions.

Since recognition of pathways involved in pathogenesis can lead to the identification of causative agents and therapeutic targets, an important avenue of research regarding chronic lung diseases is characterization of cellular and molecular abnormalities that correlate with disease presence, severity, and outcome. Powerful tools of molecular histopathology are now available that allow studies of inflammatory cell types, gene expression, protein content, cellular phenotype, and microbial and viral infection with exquisite sensitivity and high spatial resolution. The commercial availability of antibodies for routine immunohistochemistry has also increased greatly in recent years. As a result, many researchers now have the capability to examine the roles of specific pathways in pulmonary diseases through studies of lung tissues at the cellular and molecular levels.

Human lung tissues are widely available for study from excisions of lung lobes for possible cancer, lung volume reduction surgeries, lung transplantations, and video-assisted thoracic surgical lung biopsies. However, considerable expertise, expense, and effort are required for recruitment and clinical characterization of lung tissue donor subjects, lung tissue collection, and specimen processing. Processing of lung tissues for research is especially demanding since insufflation is required to preserve tissue architecture. These constraints limit the ability of many researchers, particularly basic scientists, to perform molecular histopathological research related to pulmonary diseases. The LTRC will enable mechanistic studies of disease using lung tissues by performing the prerequisite functions of donor subject recruitment and characterization and tissue collection and processing.

c. Description of Technical Requirements

The LTRC, through the Tissue Processing and Distribution Center, will facilitate histopathological research of pulmonary diseases by preparing and distributing to researchers collections of tissue specimens obtained at surgery. Collections of specimens will be linked to extensive clinical data appropriate to the specific disease. In general, donor subjects will be recruited for specific enrollment groups that are designed to address important research questions. Through this program the NHLBI expects to provide an important resource to the lung research community that will enhance elucidation of disease mechanisms and lead to better methods of preventing and managing various chronic lung diseases.

The LTRC will be comprised of up to 5 Clinical Centers (CCs), RFP–NHLBI–HR–04–08; a Tissue Processing and Distribution Center (TC), RFP–NHLBI–HR–04–09; a Radiology Center (RC), RFP–NHLBI–HR–04–10; and a Data Coordinating Center (DCC) RFP–NHLBI–HR–04–11. Offerors are strongly encouraged to read the RFPs for all of these components of the LTRC to better understand the overall structure and function of the consortium. A Steering Committee, consisting of the NHLBI Project Officer (non-voting member) and the Principal Investigator (PI) from each center awarded a contract under the above RFPs, will meet during Phase I to develop the LTRC Protocol Manual. Upon completion, the LTRC Protocol Manual will be submitted for review to an independent Scientific Advisory Committee (SAC), appointed by the NHLBI. The SAC will review the LTRC Protocol Manual and provide comments and advice to the NHLBI. During Phase II, the SAC will evaluate requests for access to LTRC resources and of research studies proposed by the CCs. An Observational Study Monitoring Board (OSMB) will be appointed by the NHLBI to monitor the protection of human research subjects and the overall progress and performance of the LTRC.

It is recognized that tissues from donor subjects with lung diseases other than COPD and idiopathic pulmonary fibrosis, especially rare conditions, would also be valuable to the lung research community. To allow for the collection and distribution of such lung tissues through the LTRC, the NHLBI intends to support collection of additional tissue specimens through a number of External Tissue Contributors (ETCs). These contributing sites will not carry out the extensive clinical characterization of donor subjects done by contracted Clinical Centers, but will provide tissue samples and clinical data extracted from the donor subjects' medical records. Proposals for ETCs will not be accepted in response to this solicitation. Centers interested in participating as an ETC are encouraged to contact the Data Coordinating Center after 8/01/2004 to obtain additional information. An ETC will be reimbursed for samples by the Data Coordinating Center using a capitated reimbursement mechanism. ETC investigators will not be represented on the LTRC Steering Committee nor will they receive funding for research studies through the LTRC.

d. Phasing

Phase I (6 months): The PI from each of the awarded Clinical Centers, the Tissue Processing and Distribution Center, the Radiology Center, and the Data Coordinating Center will meet several times to identify enrollment groups and develop the LTRC Protocol Manual.

Phase II (54 months): Clinical Center personnel will be trained in consortium operations, and investigators will recruit and enroll donor subjects and obtain tissue samples, CT scans, and clinical data in accordance with the LTRC Protocol Manual. Clinical Center investigators will forward clinical data to the Data Coordinating Center, tissue samples to the Tissue Processing and Distribution Center, and CT images to the Radiology Center. Clinical Center investigators will conduct research using the LTRC specimens and data and will prepare manuscripts and abstracts for publication and presentation.

e. Clinical Research/Human Subjects

Research involving the collection, processing and use of biological specimens, clinical data, and CT image data from humans will be proposed in response to this solicitation. The following guidelines and policies, which may be applicable to this solicitation, can be viewed at: http://www.nhlbi.nih.gov/funding/policies

- Establishing Data and Safety Monitoring Boards and Observational Study Monitoring Boards
- Guidelines for Data Quality Assurance in Clinical Trials and Observational Studies
- Responsibilities of OSMBs Appointed by the NHLBI
- NHLBI Guidelines for Implementation of the Policy on Inclusion of Minorities and Women in Study Populations
- NHLBI Guidelines for Implementation of the Policy on Inclusion of Children in Research Involving Human Subjects
- Terms and Conditions for Accrual of Research Subjects in Research Supported by NHLBI
- Reporting Clinical Study Serious Adverse Events
- Medicare Coverage of Clinical Trials
- Human Tissue Repositories—Guidelines
- Tissue Sharing in Informed Consent—Guidance

f. Special Requirements

1. OMB CLEARANCE

After the LTRC Protocol Manual has been approved, a request for clinical exemption for LTRC-generated forms will be coordinated by the NHLBI Project Officer for submission to the NIH OMB Clearance Officer. It is expected that forms used by the LTRC to collect clinical data will be exempt from OMB clearance requirements.

2. CAPITATION

A capitation reimbursement system will be discussed and developed during Phase I for the participating Clinical Centers. Capitation rates for individual Clinical Centers will be based on cost elements identifed for performance of protocol procedures. Reimbursement of capitated costs will only be made after the Data Coordinating Center has verified to the Contracting Officer that the tissue specimens, clinical data, and CT image data are complete and satisfy quality control standards of the LTRC.

3. IRB APPROVAL

All contractors will be required to obtain Institutional Review Board (IRB) approval of relevant LTRC protocols and any subsequent research protocols proposed and approved.

g. Estimate of Effort

The Government considers the types of personnel and estimated levels of effort identified below to be required for successful completion of Clinical Center objectives. Effort is shown as a percentage of FTE (full-time equivalent) labor. The personnel and levels of effort listed below are for information only and are not to be considered restrictive for proposal purposes. The levels were formulated by NHLBI staff experienced in the conduct of multi-center clinical trials, utilizing recent experience.

Labor Category	Phase I	Core Phase II	Protocol Costs Phase II
Principal Investigator	25%	25%	10%
Co–Investigator	25%	25%	0%
Clinical Research Assistant	0%	0%	100%
Clinical Coordinator	25%	25%	75%

Labor Category	Phase I	Core Phase II	Protocol Costs Phase II
Laboratory Technician	25%	25%	75%
Admin. Asst./Data Entry	25%	25%	25%
Total:	**125%**	**125%**	**285%**

During Phase I the PI from each center will meet in Bethesda, Maryland to develop the LTRC Protocol Manual. During Phase II Clinical Center (CC) staff will be trained and certified in consortium operations. CC staff will be responsible for screening and recruitment of donor subjects, and for ensuring timely completion of data forms. Specimens and data collected will be processed and provided to the appropriate LTRC center. Core Costs will provide baseline support for CC infrastructure and staff. Protocol Costs will be reimbursed using a capitated system that will take into account the number of donor subjects enrolled, the completion of protocol procedures, and the quality of samples and data obtained from each enrolled donor subject.

***Note**: Offerors shall ensure that the PI and all other personnel proposed will not be committed on Federal grants and contracts for more than a total of 100% of their time. If the situation arises where it is determined that a proposed individual is committed for more than 100% of his or her time, the Government will require action on the part of the offeror to adjust the time commitment.*

h. Travel

Travel costs should be based on Steering Committee meetings in Bethesda, Maryland and staff attending a training course at the Tissue Processing and Distribution Center.

During Phase I (6 months): Each center should propose travel costs based on two investigators attending four 2-day Steering Committee meetings in Bethesda, Maryland.

Phase II (54 months): Clinic Center staff will be trained and certified in Consortium operations. One tissue processing technician from each Clinical Center will travel to the Tissue Processing and Distribution Center to attend a training course in the first year. Two investigators will attend two 2-day Steering Committee meetings in Bethesda, Maryland each year.

i. Costs for Clinical Characterization of Donor Subjects

Clinical Characterization costs include costs associated with performance of the LTRC protocol procedures (e.g., clinical testing of donor subjects, such as administration of questionnaires, a blood draw, a CT scan, and pulmonary function testing with measurement of bronchodilator responses and CO diffusing capacity). Patient care costs that are considered routine care, and covered by third party coverage, will not be reimbursed with contract funds and should be excluded from the cost proposal.

For the purpose of this solicitation, offerors included in the competitive range may be required to submit additional cost or pricing information substantiating their proposed patient care related costs. This additional information will be requested after establishment of the competitive range.

j. Consortium Committees

The **Steering Committee**, consisting of the NHLBI Project Officer and the PI from each participating center, will work together during Phase I to: 1) define enrollment groups of donor subjects useful for testing hypotheses regarding the etiology and/or pathogenesis of COPD or idiopathic pulmonary fibrosis; 2) establish inclusion/exclusion criteria for enrollment groups based on characteristics that can be determined prior to surgery and without clinical testing; 3) determine a target number of donor subjects to be recruited in each enrollment group; 4) finalize the LTRC Protocol Manual, and 5) provide scientific

direction to the LTRC at an operational level. During Phase I, the Steering Committee will meet approximately monthly, including four meetings and teleconferences as needed. During Phase II the Steering Committee will meet twice a year and conduct teleconferences as needed. Each participating center will have one vote on issues pertaining to the LTRC.

A **Scientific Advisory Committee** (SAC), appointed by the NHLBI, will make recommendations to the NHLBI regarding the consortium protocols. The SAC will review the LTRC Protocol Manual and amendments thereto regarding feasibility and potential for accomplishing LTRC objectives. The SAC will also evaluate research proposals involving LTRC specimens and clinical data. The SAC will meet twice during Phase 1 and once per year thereafter and will conduct teleconferences as needed.

An **Observational and Study Monitoring Board** (OSMB) will be established to monitor overall progress, data outcomes, and patient safety. The Board will periodically evaluate consortium procedures, review results for adverse events, and advise the NHLBI when changes should be made. The Board will meet once per year and conduct teleconferences as needed. Responsibilities of OSMBs appointed by the NHLBI can be found at: http://www.nhlbi.nih.gov/funding/policies/osmb_inst.htm

k. Past Performance

Offerors shall submit the following information as part of their business proposal (for both the offeror and proposed major subcontractors): A list of the contracts, grants, or cooperative agreements completed during the past two (2) years and all contracts currently in progress for products or services similar to the solicitation workscope. The list may include agreements entered into with the Federal Government, agencies of state and local governments, and commercial organizations. Offerors that are newly formed entities without prior contracts should list contracts and subcontracts performed by all proposed key personnel. Include the following information for each contract or subcontract:

1. Name of Contracting Organization
2. Contract Number (for subcontracts, provide the prime contract number and subcontract number)
3. Contract Type
4. Total Contract Value
5. Description of Requirement
6. Contracting Officer's Name, Telephone Number, and E-mail Address
7. Project Officer's Name, Telephone Number, and E-mail Address

Each offeror will be evaluated on its performance under existing and prior contracts for similar products or services. Performance information will be used for responsibility determinations. The Government will focus on information that demonstrates quality of performance relative to the size and complexity of the acquisition under consideration. The Government is not required to contact all references provided by the offeror. References other than those identified by the offeror may be contacted by the Government to obtain additional information that will be used in the evaluation of an offeror's past performance.

l. Offerors Must Address

In order to expedite finalization of the LTRC Protocol Manual and research plans within the Phase I time line, offerors shall:

1. Demonstrate access to donor subjects and ability to obtain tissue specimens from 36-72 (3-6 per month) appropriate patients per year. Provide detailed plans for identification and recruitment of donor subjects. Identify the numbers of potential tissue donor subjects with idiopathic pulmonary fibrosis and/or COPD and characterize the potential donor subject populations in terms of disease severity, co-morbid conditions, surgical procedure (resection for possible lung cancer, lung volume reduction surgery, lung transplant, etc.), gender, and racial/ethnic minority status. Document previous

success in obtaining specimens, for research purposes, from COPD and idiopathic pulmonary fibrosis patients. Documentation of access to patients may include a discussion of research studies at the offeror's institution that could provide suitable donor subjects.

Note: Offerors that do not have prior experience in obtaining tissue specimens at the projected rate shall describe plans to meet the target enrollment goals.

2. Document potential tissue donor subjects appropriate as controls (resection for possible lung cancer, lung transplant, video-assisted thoracic surgical lung biopsy, etc.) for studies of COPD or idiopathic pulmonary fibrosis. Characterize this potential donor subject population in terms of medical diagnoses, surgical procedure, age, gender, and racial/ethnic minority status. Describe previous success in recruiting tissue donor subjects from this population.

3. Propose approaches for clinical characterization of donor subjects with COPD, including data to be extracted from the medical record, questionnaires, and laboratory tests (e.g., pulmonary function testing, testing of airway reactivity, chest CT imaging).

4. Propose approaches for clinical characterization of donor subjects with idiopathic pulmonary fibrosis, including data to be extracted from the medical record, questionnaires, and laboratory tests (e.g., pulmonary function testing, chest CT imaging).

5. Address willingness to interact effectively with the Data Coordinating Center to transmit and validate clinical data, with the Radiology Center to transmit CT image data, and with the Tissue Processing and Distribution Center to process and transmit biological specimens.

6. Provide detailed plans for assuring the protection and privacy of human research subjects. Provide documentation of an Office of Human Research Protections–approved assurance (e.g., a Federal Wide Assurance).

7. Document experience and expertise in the collection of clinical data and transmission of the data to a Data Coordinating Center.

8. Provide letters of commitment from surgeons documenting their willingness to cooperate in the harvest and rapid processing of lung tissues for research purposes.

9. Propose two research studies of COPD and/or idiopathic pulmonary fibrosis using LTRC specimens and data. The research studies (each not to exceed 6 single-sided pages as a part of the technical proposal) should include the hypotheses or questions to be addressed, the background and rationale of the proposed studies, preliminary data, the donor subject groups to be studied, the numbers of donor subjects per group, the types of specimen preparations required, the experimental approaches and methods to be employed, and the significance of the anticipated results. Offerors may assume availability in each experimental group of five times the number of donor subjects expected to be recruited for each enrollment group at the offeror site. For purposes of developing research plans, offerors may assume that the Tissue Processing and Distribution Center will prepare and make available specimens in all of the following formats a) microarrays of frozen sections of lung tissues insufflated with imbedding medium, b) microscope slides with frozen sections of lung appropriate for laser capture microdissection, c) aliquots of total RNA derived from lung tissues initially frozen in liquid nitrogen, d) aliquots of random hexamer-primed cDNA produced from lung tissue, e) aliquots of total protein derived from lung tissues initially frozen in liquid nitrogen, f) aliquots of plasma, g) genomic DNA, and h) cryopreserved blood lymphocytes. Offerors may assume that the Radiology Center will provide histograms of lung radiographic density for each donor subject and that the Tissue Processing and Distribution Center will provide digital images of histological sections and data on mean chord length (a measure of alveolar size) in glutaraldehyde-fixed lung tissue blocks adjacent to

those tissues from which frozen sections are obtained. Offerors may assume that up to $112,500 total costs per year, per Clinical Center, will be available for the support of research studies, beginning in year 2. The $112,500 is only an estimate; the final amount will vary depending on scope and negotiations. All research studies will undergo peer review during Phase II by the SAC. Funding will not occur until NHLBI has provided approval. Funding for research studies may be provided as a performance incentive. Offerors should prepare a separate one page spread sheet detailing the total cost of performance, by category, for each research study proposed. Research study costs should not be commingled with the LTRC cost proposal.

10. The proposed PI should have leadership experiences and be available to participate in Steering Committee activities. It is expected that the PI will be an established investigator who has clinical expertise in caring for patients with COPD or idiopathic pulmonary fibrosis and who has participated in multi-center clinical studies. Prior experience in enrolling patients in multi-center studies will be an important guide for determining the potential of the offeror to successfully fulfill the requirements of this solicitation. Discuss the qualifications and experience of the PI, proposed investigators, and key staff.

11. Document experience of proposed key personnel and staff in molecular and histopathological research of lung diseases.

12. Provide a detailed description of laboratory/clinical facilities available to conduct the Statement of Work. The description should identify resources to 1) process tissue specimens prior to their transfer to the Tissue Processing and Distribution Center, 2) obtain research CT scans and transmit CT images electronically to the Radiology Center, and 3) perform clinical testing, administer questionnaires and transmit data electronically to the Data Coordinating Center.

    Note: *Offerors from institutions that have a General Clinical Research Center (GCRC) funded by the NIH National Center for Research Resources may wish to identify the GCRC as a resource for the proposed research. In such a case, a letter of agreement from the GCRC Program Director and the PI shall be included with the technical proposal. Clear distinction should be made in the proposal between tasks and facilities funded by the GCRC and those requiring reimbursement under this contract.*

13. Describe the administrative structure of the proposed Clinical Center.

14. Describe any institutional commitments that will be provided if selected for award.

15. Provide any other information needed to allow reviewers to judge the capability of the offeror to accomplish the Statement of Work of a Clinical Center.

16. ***Note****: In order to maintain the integrity and utility of the tissue specimens, expedited transport to the Tissue Processing and Distribution Center will be required. Offerors must address plans for packaging and shipping tissue specimens so they are received at the Tissue Processing and Distribution Center within 24 hours of shipment. For proposal purposes, it should be assumed that the Tissue Processing and Distribution Center will be located in the continental United States.*

m. Information Technology Systems Security Plan

Information technology services will be used to accomplish the project objectives. The Clinical Centers may be required to submit an information technology system security plan. A decision regarding the aforementioned plan will be made during the development of the LTRC Protocol Manual.

ARTICLE C.1.—STATEMENT OF WORK

Independently and not as an agent of the Government, the Contractor shall furnish all the necessary services,

qualified personnel, material, equipment, and facilities, not otherwise provided by the Government as needed to perform the Statement of Work below. The Contractor shall deliver the items specified in ARTICLE C.2. to the destination indicated in ARTICLE F.1.

Clinical Centers (CC) will recruit and enroll specimen donor subjects; perform clinical testing of donor subjects; extract data from the patients' medical records; obtain lung tissues and other specimens and perform initial processing of these specimens; and transmit clinical data, computed tomography (CT) image data, and biological specimens to centralized facilities of the LTRC. In addition, each CC will pursue hypothesis-oriented, tissue-based research, using LTRC resources, that addresses pathogenetic mechanisms involved in COPD and/or idiopathic pulmonary fibrosis. Each CC shall perform the following tasks:

Phase I (01/30/2004 to 07/31/2004, 6 Months)

1. The PI shall have expertise in the pathogenesis of COPD and/or idiopathic pulmonary fibrosis and participate fully in the activities of the Steering Committee. The Steering Committee will develop the Lung Tissue Research Consortium Protocol Manual that establishes:

    a. Groups of donor subjects to be enrolled (selected for testing hypotheses regarding the etiology and/or pathogenesis of COPD or idiopathic pulmonary fibrosis). Inclusion/exclusion criteria for enrollment groups based on characteristics that can be determined prior to surgery and without clinical testing. Target numbers of donor subjects to be recruited in each enrollment group. Tissues to be collected (e.g., lung parenchyma, blood), clinical testing to be performed (e.g., pulmonary function testing, chest computed tomography (CT)), and data to be collected or extracted from the donor subjects' medical records (e.g., medical diagnoses, previous spirometry, pathology reports, questionnaires) for each enrollment group.

    b. Protocols for chest CT imaging and for specimen processing and transport. Protocols and forms for donor subject screening, for clinical characterization, and for data entry and transmission. Protocols for clinical data, CT image, and biological specimen quality control/quality assurance/quality rating.

2. Develop an informed consent form that provides for 1) performance of consortium procedures; 2) compilation of clinical data from the donor subjects' medical records; 3) collection of blood; 4) procurement of lung tissue specimens excised for diagnostic or therapeutic purposes; and 5) future public use of these specimens and data for unspecified lung disease research purposes, including genetic studies.

3. Work with the Data Coordinating Center to submit the LTRC Protocol Manual, and any amendments thereto, to the Scientific Advisory Committee (SAC) for review and comment. The Protocol Manual shall be finalized and submitted to the SAC no later than June 30, 2004. The SAC members, appointed by the NHLBI, will make recommendations to the NHLBI regarding the final consortium protocols. The contractor shall not begin work on Phase II activities until the NHLBI has approved the LTRC Protocol Manual and written approval has been received from the Contracting Officer.

4. Work with the Data Coordinating Center to submit the informed consent form to the Observational Study Monitoring Board (OSMB) for review and approval.

5. Obtain IRB approval for relevant procedures in the LTRC Protocol Manual, and any amendments thereto.

Phase II (08/01/2004 to 01/29/2009, 4 years 6 months)

In accordance with the LTRC Protocol Manual the contractor shall:

1. Obtain training of appropriate staff in LTRC protocols and procedures, including: 1) collection, processing, and shipping of specimens to the Tissue Processing and Distribution Center; 2) imaging procedures and transmission of CT scans to the Radiology Center, and 3) administration of questionnaires, performance

of clinical testing, extraction of clinical data from medical records, data entry, and transmission of clinical data to the Data Coordinating Center.

2. Identify potential donor subjects, obtain their informed consent, and collect screening data necessary to determine eligibility for participation. Submit screening data, including gender and ethnic/racial minority classification, to the Data Coordinating Center for verification of donor subject eligibility.

3. Recruit and enroll the number of donor subjects prescribed. Perform clinical testing and collect donor subject data as specified and transmit the data to the responsible LTRC center. Retain hard copy originals of data collection forms in a secure archive.

4. Procure biological specimens from enrolled donor subjects. Perform initial specimen processing. Transmit processed biological specimens to the Tissue Processing and Distribution Center.

5. Acquire CT images and transmit to the Radiology Center.

6. Perform quality control and quality assurance activities.

7. Report adverse events (consistent with NHLBI/NIH policies).

8. Provide reports of any radiographic or pathological abnormalities noted by the Radiology Center and/or Tissue Processing and Distribution Center to the donor subjects' primary care physicians. Inform the Data Coordinating Center when notification is accomplished.

9. The PI shall participate fully in the activities of the Steering Committee to:

    a. Identify lung conditions other than COPD and idiopathic pulmonary fibrosis for which lung tissues are needed for research and may be available from External Tissue Contributors (ETCs). Define inclusion/exclusion criteria for auxiliary groups of donor subjects appropriate for research of these conditions, set target numbers of donor subjects for each group, determine what tissues are to be accepted (e.g., surgical specimens, transbronchial biopsies), and determine what data should be extracted from the donor subjects' medical records in each of these groups.

    b. Identify any problems with existing LTRC procedures and any difficulties that may interfere with LTRC objectives. Devise strategies to improve procedures and overcome difficulties. Submit recommended changes in policies and protocols to the Scientific Advisory Committee for evaluation.

10. Develop research studies that address the etiology or pathogenesis of COPD and/or idiopathic pulmonary fibrosis using molecular or histopathological approaches and LTRC specimens and data. Work with the Data Coordinating Center to submit research proposals to the Scientific Advisory Committee for review and comment. Research studies shall not proceed until written approval has been provided by the Contracting Officer.

11. Conduct approved research studies and disseminate the results and conclusions to the research community.

ARTICLE C.2.—REPORTING REQUIREMENTS

Technical Progress Reports

In addition to those reports required by the other terms of this contract, the Contractor shall prepare and submit the following reports in the manner stated below and in accordance with ARTICLE F.1. DELIVERIES of this contract.

a. Semi-Annual Progress Report: A comprehensive Semi-annual Progress Report reflecting all activities conducted during the reporting period. The report, in a narrative form, shall be concise and informational. Extensive reference material is not desired, but such references as are necessary to full understanding may

be included. The report shall be written in sufficient detail to allow use as a reference document. The Semi-annual Progress Report shall include but not be limited to:

i. A cover page containing the following information:
    1. Contract number
    2. Contractor's name and address
    3. Principal investigator
ii. Description of overall progress.
iii. Current problems which may impede performance and proposed corrective actions.
iv. The number of donor subjects enrolled by enrollment group, gender, and ethnic/racial minority status and the extent of completion of consortium protocols on each enrolled donor subject.
v. Progress made in scientific research, including a list manuscripts published or accepted for publication related to LTRC objectives.
vi. Work to be performed during the next year.

A Semi-annual Progress Report will not be required for the period when the Final Report is due.

b. Abstracts and manuscripts published or accepted for publication shall be provided in accordance with the LTRC Protocol Manual.

c. Final Report: This report shall include a summation of the work performed and results achieved for the entire contract period of performance. The report shall be in sufficient detail to describe comprehensively the results achieved.